

Rec'd PCTO 08 JUN 2003

10/537858

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 2003/001910

A. CLASSIFICATION OF SUBJECT MATTER

IPC7: A61K 9/20, A61K 47/38, A61K 31/5377, A61P 25/00
 According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC7: A61K, A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

SE, DK, FI, NO classes as above

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CHEM.ABS.DATA, EMBASE DATA, BIOSIS DATA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|-----------|--|-----------------------|
| X | US 6228857 B1 (STEFAN BERG ET AL), 8 May 2001 (08.05.2001), column 4, line 44 - column 5, line 4, examples 16-18, claims 6-8 -- | 1-29 |
| X | US 6159971 A (STEFAN BERG ET AL), 12 December 2000 (12.12.2000), column 4, line 39 - column 5, line 4 -- | 1-29 |
| X | EP 1327440 A1 (SUMITOMO PHARMACEUTICALS COMPANY, LIMITED), 16 July 2003 (16.07.2003), claim 1, examples tables 20, 24, 28 -- | 1-29 |

 Further documents are listed in the continuation of Box C. See patent family annex.

| | |
|--|--|
| * Special categories of cited documents: | |
| "A" | document defining the general state of the art which is not considered to be of particular relevance |
| "E" | earlier application or patent but published on or after the international filing date |
| "L" | document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) |
| "O" | document referring to an oral disclosure, use, exhibition or other means |
| "P" | document published prior to the international filing date but later than the priority date claimed |
| "T" | later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention |
| "X" | document of particular relevance: the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone |
| "Y" | document of particular relevance: the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art |
| "&" | document member of the same patent family |

Date of the actual completion of the international search

19 April 2004

Date of mailing of the international search report

20-04-2004

Name and mailing address of the ISA/
 Swedish Patent Office
 Box 5055, S-102 42 STOCKHOLM
 Facsimile No. +46 8 666 02 86

Authorized officer

EVA JOHANSSON/BS
 Telephone No. +46 8 782 25 00

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 2003/001910

| C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT | | |
|---|--|-----------------------|
| Category* | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
| X | PATENT ABSTRACTS OF JAPAN vol., 1998, no.10, 31 August 1998 (1998-08-31) & JP 10114655 A (KYOWA HAKKO KOGYO CO LTD), 6 May 1998 (1998-05-06) abstract -- | 1-29 |
| A | WO 0236126 A1 (LUPIN LIMITED), 10 May 2002 (10.05.2002) -- | 1-29 |
| A | EP 0533268 A1 (GLAXO GROUP LIMITED), 24 March 1993 (24.03.1993) -- ----- | 1-29 |

INTERNATIONAL SEARCH REPORT
Information on patent family members

31/03/2004

International application No.
PCT/SE 2003/001910

| | | | | | | | |
|----|---------|----|------------|----|------------|---|------------|
| US | 6228857 | B1 | 08/05/2001 | AU | 2337400 | A | 07/08/2000 |
| | | | | BR | 0007577 | A | 23/10/2001 |
| | | | | CA | 2359105 | A | 27/07/2000 |
| | | | | CN | 1337956 | T | 27/02/2002 |
| | | | | CZ | 20012643 | A | 16/01/2002 |
| | | | | EE | 200100381 | A | 16/12/2002 |
| | | | | EP | 1149083 | A | 31/10/2001 |
| | | | | HU | 0200412 | A | 29/06/2002 |
| | | | | ID | 30556 | A | 00/00/0000 |
| | | | | IL | 144444 | D | 00/00/0000 |
| | | | | JP | 2002535320 | T | 22/10/2002 |
| | | | | NO | 20013601 | A | 11/09/2001 |
| | | | | NZ | 512684 | A | 30/06/2003 |
| | | | | PL | 349775 | A | 09/09/2002 |
| | | | | SE | 9900190 | D | 00/00/0000 |
| | | | | SK | 10222001 | A | 05/03/2002 |
| | | | | TR | 200102087 | T | 00/00/0000 |
| | | | | US | 6291458 | B | 18/09/2001 |
| | | | | WO | 0043378 | A | 27/07/2000 |
| | | | | ZA | 200105491 | A | 03/10/2002 |
| | | | | SE | 0000079 | D | 00/00/0000 |
| | | | | SE | 0100048 | A | 14/07/2001 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE 2003/001910

| | | | | | | | |
|----|---------|----|------------|----|------------|-----|------------|
| US | 6159971 | A | 12/12/2000 | AT | 240733 | T | 15/06/2003 |
| | | | | AU | 752722 | B | 26/09/2002 |
| | | | | AU | 9193098 | A | 05/04/1999 |
| | | | | BR | 9812088 | A | 26/09/2000 |
| | | | | CA | 2302382 | A | 25/03/1999 |
| | | | | CN | 1278729 | T | 03/01/2001 |
| | | | | DE | 69814882 | D | 00/00/0000 |
| | | | | DK | 1014985 | T | 15/09/2003 |
| | | | | EE | 4141 | B | 15/10/2003 |
| | | | | EE | 200000141 | A | 15/02/2001 |
| | | | | EP | 1014985 | A,B | 05/07/2000 |
| | | | | SE | 1014985 | T3 | |
| | | | | ES | 2200370 | T | 01/03/2004 |
| | | | | HK | 1032739 | A | 00/00/0000 |
| | | | | HU | 0200602 | A | 29/07/2002 |
| | | | | IL | 134776 | D | 00/00/0000 |
| | | | | JP | 2001516718 | T | 02/10/2001 |
| | | | | NO | 20001399 | A | 10/05/2000 |
| | | | | NZ | 503171 | A | 01/02/2002 |
| | | | | PL | 339371 | A | 18/12/2000 |
| | | | | PT | 1014985 | T | 31/10/2003 |
| | | | | SE | 9703375 | D | 00/00/0000 |
| | | | | SI | 1014985 | T | 00/00/0000 |
| | | | | SK | 2852000 | A | 12/09/2000 |
| | | | | TR | 200000727 | T | 00/00/0000 |
| | | | | WO | 9913877 | A | 25/03/1999 |
| | | | | ZA | 9807817 | A | 18/03/1999 |
| | | | | AT | 242463 | T | 15/06/2003 |
| | | | | CA | 2331174 | A | 18/11/1999 |
| | | | | DE | 69908582 | D | 00/00/0000 |
| | | | | EP | 1075637 | A,B | 14/02/2001 |
| | | | | IL | 139216 | D | 00/00/0000 |
| | | | | NO | 20005620 | A | 07/11/2000 |
| | | | | SE | 510581 | C | 07/06/1999 |
| | | | | SE | 9801601 | A | 07/06/1999 |
| | | | | US | 6446536 | B | 10/09/2002 |
| | | | | WO | 9958921 | A | 18/11/1999 |
| EP | 1327440 | A1 | 16/07/2003 | AU | 8623701 | A | 02/04/2002 |
| | | | | CA | 2424001 | A | 20/03/2003 |
| | | | | US | 2004028741 | A | 12/02/2004 |
| | | | | WO | 0224166 | A | 28/03/2002 |
| WO | 0236126 | A1 | 10/05/2002 | AU | 7867301 | A | 15/05/2002 |
| | | | | EP | 1330250 | A | 30/07/2003 |
| | | | | US | 2002119195 | A | 29/08/2002 |

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2003/001910

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: **20–25**
because they relate to subject matter not required to be searched by this Authority, namely:
see extra sheet

2. Claims Nos.: **1 and 2**
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
see extra sheet

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see extra sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1–29

Remark on Protest

- The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2003/001910

Box II.1

Claims 20-25 and 27 relate to methods of treatment of the human or animal body by surgery or by therapy or diagnostic methods practiced on the human or animal body (PCT Rule 39.1(iv)). Nevertheless, a search has been executed for these claims. The search has been based on the alleged effects of the compounds or compositions.

Box II.2

The expressions "disintegrant", "soluble filler" and "binder" in claims 1 and 2 do not allow a complete search of the full scope of the expressions in question. The present wording of the claim cannot be considered to fulfill the requirements of clarity and conciseness (article 6 PCT). Therefore the search has been based on the substances mentioned in claims 5, 7 and 9.

Box III

The International Search Authority considers that there are three inventions covered by the claims indicated as follows:

I: Claims: 1-28 (partially) and 29 directed to an oral immediate release dosage form comprising *N*-[5-methyl-8-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydro-2-naphtyl]-4-morpholinobenzamide or its salts (or other active compounds that forms an agglomerate upon contact with water-claim 29) and at least one disintegrant and optionally at least one soluble filler and/or one binder.

II: Claims 1-4, 7-14, 16-18 and 20-28 (all partially) directed to an oral immediate release dosage form comprising *N*-[5-methyl-8-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydro-2-naphtyl]-4-morpholinobenzamide or its salts and at least one soluble filler and optionally a binder.

III: Claims 2-4, 9-14, 17-18 and 20-28 (all partially) directed to an oral immediate release dosage form comprising *N*-[5-methyl-8-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydro-2-naphtyl]-4-morpholinobenzamide or its salts and at least one binder.

The ISA has carried out a partial search which relates to invention I mentioned above.

The applicant is invited to pay two additional fees for each of the inventions II-III as listed above.

.../...

INTERNATIONAL SEARCH REPORT

International application No.
PCT/SE2003/001910

The present application has been considered to contain three inventions which are not linked such that they form a single general inventive concept, as required by Rules 13.1, 13.2 and 13.3 PCT for the following reasons:

The three inventions all relate to the problem of providing an oral immediate release dosage form comprising *N*-[5-methyl-8-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydro-2-naphthyl]-4-morpholinobenzamide or its salts. However the application provides three different kinds of dosage forms comprising different excipients namely:

The subject matter defined as invention I above relates to an oral immediate release dosage form comprising the active compound and at least one disintegrant.

The subject matter defined as invention II above relates to an oral immediate release dosage form comprising the active compound and at least one soluble filler.

The subject matter defined as invention III above relates to an oral immediate release dosage form comprising the active compound and at least one binder.

The features that these different formulations have in common are that they are oral immediate release dosage forms comprising *N*-[5-methyl-8-(4-methylpiperazin-1-yl)-1,2,3,4-tetrahydro-2-naphthyl]-4-morpholinobenzamide or its salts. Such dosage forms are however known from US 6,228,857 B1. Hence the claims are not linked by any common special technical feature apart from the prior art. Consequently, the requirements of Rules 13.1 and 13.2 PCT are not met.

Only invention I (claims 1-28 (partially) and 29) has been search.

INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.

31/03/2004

PCT/SE 2003/001910

| | | | | | | | |
|----|---------|----|------------|----|----------|-----|------------|
| EP | 0533268 | A1 | 24/03/1993 | SE | 0533268 | T3 | |
| AP | | | | AP | 303 | A | 28/01/1994 |
| AP | | | | AP | 9200427 | D | 00/00/0000 |
| AT | | | | AT | 204262 | T | 15/09/2001 |
| AU | | | | AU | 656021 | B | 19/01/1995 |
| AU | | | | AU | 2453092 | A | 25/03/1993 |
| CA | | | | CA | 2078505 | A | 19/03/1993 |
| CN | | | | CN | 1071919 | A | 12/05/1993 |
| CZ | | | | CZ | 9202854 | A | 14/04/1993 |
| DE | | | | DE | 69232003 | D,T | 25/04/2002 |
| DK | | | | DK | 533268 | T | 03/12/2001 |
| ES | | | | ES | 2162792 | T | 16/01/2002 |
| FI | | | | FI | 924160 | A | 19/03/1993 |
| GB | | | | GB | 9119931 | D | 00/00/0000 |
| HU | | | | HU | 65608 | A | 28/07/1994 |
| HU | | | | HU | 9202968 | D | 00/00/0000 |
| IL | | | | IL | 103198 | A | 18/06/1996 |
| JP | | | | JP | 3295143 | B | 24/06/2002 |
| JP | | | | JP | 6116251 | A | 26/04/1994 |
| MX | | | | MX | 9205280 | A | 01/03/1993 |
| NO | | | | NO | 923618 | A | 19/03/1993 |
| NZ | | | | NZ | 244373 | A | 28/03/1995 |
| OA | | | | OA | 10049 | A | 14/10/1996 |
| PL | | | | PL | 295960 | A | 06/09/1993 |
| PT | | | | PT | 533268 | T | 28/02/2002 |
| RU | | | | RU | 2077535 | C | 20/04/1997 |
| US | | | | US | 5340810 | A | 23/08/1994 |
| US | | | | US | 5510350 | A | 23/04/1996 |
| ZA | | | | ZA | 9207108 | A | 08/09/1993 |
| CN | | | | CN | 1076195 | A | 15/09/1993 |
| GB | | | | GB | 9205338 | D | 00/00/0000 |